



General

Guideline Title

KDOQI clinical practice guideline for diabetes and CKD: 2012 update

Bibliographic Source(s)

National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. Am J Kidney Dis. 2012 Nov;60(5):850-86. [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. Am J Kidney Dis. 2007 Feb;49(2 Suppl 2):S12-154.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [April 8, 2016 – Metformin-containing Drugs](#) : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.

Recommendations

Major Recommendations

Note from the National Kidney Foundation (NKF) and the National Guideline Clearinghouse (NGC): The 2012 update to the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for Diabetes and CKD provides updated recommendations for management of hyperglycemia, dyslipidemia, and albuminuria in individuals with diabetes mellitus and chronic kidney disease (CKD). Guideline

recommendations for screening and diagnosis, management of hypertension, nutritional management, multifaceted approach to intervention, diabetes and CKD in special populations, and self-management were not updated. These recommendations can be found in the 2007 guideline (see the "Availability of Companion Documents" field), which is available from the [National Kidney Foundation Web site](#)

Definitions for the strength of recommendations (1,2) and the quality of the supporting evidence (A-D) as well as additional considerations, are provided at the end of the "Major Recommendations" field.

Clinical Practice Guidelines (CPGs) for Diabetes and Chronic Kidney Disease (CKD)

Guideline 2: Management of Hyperglycemia and General Diabetes Care in CKD

Hyperglycemia, the defining feature of diabetes, is a fundamental cause of vascular target organ complications, including diabetic kidney disease (DKD). Intensive treatment of hyperglycemia prevents elevated albuminuria or delays its progression, but patients treated by approaches designed to achieve near normal glycemia may be at increased risk of severe hypoglycemia. Evidence that intensive treatment has an effect on loss of glomerular filtration rate (GFR) is sparse.

2.1: The Work Group recommends a target hemoglobin A_{1c} (HbA_{1c}) of ~7.0% to prevent or delay progression of the microvascular complications of diabetes, including DKD. (1A)

2.2: The Work Group recommends not treating to an HbA_{1c} target of <7.0% in patients at risk of hypoglycemia. (1B)

2.3: The Work Group suggests that target HbA_{1c} be extended above 7.0% in individuals with co-morbidities or limited life expectancy and risk of hypoglycemia. (2C)

Guideline 4: Management of Dyslipidemia in Diabetes and CKD

Dyslipidemia is common in people with diabetes and CKD. Cardiovascular events are a frequent cause of morbidity and mortality in this population. Lowering low-density lipoprotein cholesterol (LDL-C) with statin-based therapies reduces risk of major atherosclerotic events, but not all-cause mortality, in patients with CKD including those with diabetes.

4.1: The Work Group recommends using LDL-C lowering medicines, such as statins or statin/ezetimibe combination, to reduce risk of major atherosclerotic events in patients with diabetes and CKD, including those who have received a kidney transplant. (1B)

4.2: The Work Group recommends not initiating statin therapy in patients with diabetes who are treated by dialysis. (1B)

Guideline 6: Management of Albuminuria in Normotensive Patients with Diabetes

Treatments that produce a lasting decrease in urinary albumin excretion may slow the progression of DKD even in the absence of hypertension. However, most people with diabetes and albuminuria have hypertension. Assessment of albuminuria is addressed in Guideline 1 ([2007 KDOQI Diabetes Guideline](#)). Management of hypertension is addressed in Guideline 3 ([2007 KDOQI Diabetes Guideline](#)) and the NGC summary of [KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease](#).

6.1: The Work Group recommends not using an angiotensin-converting enzyme inhibitor (ACE-I) or an angiotensin receptor blocker (ARB) for the primary prevention of DKD in normotensive normoalbuminuric patients with diabetes. (1A)

6.2: The Work Group suggests using an ACE-I or an ARB in normotensive patients with diabetes and albuminuria levels ≥ 30 mg/g who are at high risk of DKD or its progression. (2C)

Definitions:

Grade for Strength of Recommendation in the Diabetes and CKD Guideline

Guideline statements have evolved since the publication of the original diabetes guideline. The moral imperative that clinicians "should" implement a particular treatment was replaced by "The Work Group recommends" if the strength of the recommendation was strong or moderately strong and "The Work Group suggests" if the strength of the recommendation was weak. This change was made to reflect the uncertainties inherent to all research findings and the need to adjust any recommendations to the needs of the individual patient.

	Implications		
Grade*	Patients	Clinicians	Policy
Level 1 "The Work Group recommends"	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 "The Work Group suggests"	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

*The additional category "Not Graded" is used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding monitoring intervals, counseling, and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

Grade for Quality of Evidence in the Diabetes and Chronic Kidney Disease (CKD) Guideline

Grade	Quality of Evidence	Meaning
A	High	The Work Group is confident that the true effect lies close to that of the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of effect is very uncertain, and often will be far from the truth.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Diabetes mellitus/p>

Other Disease/Condition(s) Addressed

Chronic kidney disease stages 1 to 5

Guideline Category

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Cardiology

Endocrinology

Family Practice

Geriatrics

Internal Medicine

Nephrology

Nursing

Obstetrics and Gynecology

Pediatrics

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

- To assist the practitioner caring for patients with diabetes and chronic kidney disease (CKD) by reviewing substantial high-quality new evidence since the original 2007 Kidney Disease Outcomes Quality Initiative (KDOQI) guideline
- To specifically address hemoglobin A_{1c} (HbA_{1c}) targets, treatments to lower low-density lipoprotein cholesterol (LDL-C) levels, and use of angiotensin-converting enzyme inhibitor (ACE-I) and angiotensin receptor blocker (ARB) treatment in diabetic patients with and without albuminuria

Target Population

Patients with diabetes mellitus with or without chronic kidney disease (CKD) stages 1 to 5, including dialysis and transplant patients

Interventions and Practices Considered

1. Targeted hemoglobin A_{1c} (HbA_{1c}) of ~7.0% to prevent or delay progression of the microvascular complications of diabetes, including diabetic kidney disease (DKD)
2. Use of low-density lipoprotein cholesterol (LDL-C) lowering medicines, such as statins or statin/ezetimibe combination, to reduce risk of major atherosclerotic events (Note: statins are not recommended in patients who are treated by dialysis)

3. Use of an angiotensin-converting enzyme inhibitor (ACE-I) or an angiotensin receptor blocker (ARB) in normotensive patients with diabetes and albuminuria levels ≥ 30 mg/g

Major Outcomes Considered

- Primary outcome: all-cause mortality
- Secondary health outcomes:
 - End-stage renal disease (ESRD)
 - Cardiovascular death
 - Nonfatal cardiovascular events
 - Clinically significant retinopathy including vision loss
 - Amputations
 - Symptomatic hypoglycemia of sufficient severity to require the assistance of another person
- Intermediate outcomes:
 - Changes in the level of albuminuria and glomerular filtration rate
 - Doubling of serum creatinine (SCr) concentration
 - Progression to chronic kidney disease (CKD) stage 4 or higher

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

MEDLINE was searched to identify randomized controlled trials published between January 2003 and October 2010 that related to albuminuria, glycemic and lipid management in patients with diabetes. All titles and abstracts were assessed for their appropriateness to address key questions that were developed by the multidisciplinary team and outlined below. Study reference lists, reviews, and meta-analyses were evaluated and references to other clinical trials were elicited from members of the Work Group.

Key questions (KQ) to be addressed by the evidence review:

KQ 1: In patients with diabetes (type 1 or 2), with or without chronic kidney disease (CKD), does intensive glycemic control (as defined by lower target glycosylated hemoglobin) improve health outcomes compared to controls?

KQ 2: What harms result from more intense glycemic control in individuals with diabetes (type 1 or 2)?

KQ 3: In patients with diabetes (type 1 or 2) and CKD, what evidence is there for specific lipid management targets (defined as goals for total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], triglycerides) that improve health outcomes?

KQ 4: Is there evidence for specific lipid altering agent use for patients with diabetes (type 1 or 2) and CKD?

KQ 5: What harms result from more intense lipid management or use of specific lipid altering agents in individuals with diabetes (type 1 or 2) and CKD?

KQ 6: What interventions prevent incident albuminuria and/or progression of albuminuria in patients with diabetes in whom further reduction in blood pressure is not the specific treatment objective?

KQ 7: Is albuminuria a valid surrogate for health outcomes in diabetes?

See the systematic review document (see the "Availability of Companion Documents" field) for more information.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grade for Quality of Evidence in the Diabetes and Chronic Kidney Disease (CKD) Guideline

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Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data from each study that pertained to study quality, trial characteristics, population characteristics, efficacy, outcomes, withdrawals, and adverse events were extracted. Evidence tables were created to address the key questions. Study quality was rated as good, fair, or poor according to criteria suggested by the Cochrane Collaboration, and included information on adequate allocation concealment, method of blinding, use of the intention-to-treat principle for data analysis, reporting of dropouts, and reasons for attrition.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The guideline update effort was a voluntary and multidisciplinary undertaking that included input from National Kidney Foundation (NKF) scientific staff, an evidence review team from the Minneapolis Veterans Administration Center for Chronic Disease Outcomes Research, and a Work Group of experts in relevant disciplines.

In formulating the guideline statements, separate recommendation levels (1 or 2) were assigned for each specific recommendation based on the overall strength of the recommendation and separate letter grades (A, B, C, or D) were assigned based on the overall quality of the evidence for a particular intervention and outcome (see the "Rating Scheme for the Strength of the Recommendations" and the "Rating Scheme for the Strength of the Evidence" fields). *Strength of guideline recommendations* was determined by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach used by Kidney Disease: Improving Global Outcomes (KDIGO). The overall quality and strength of evidence was assessed using methodology developed by the Agency for Healthcare Research and Quality and the Effective Health Care Program. *Quality*

of evidence ratings included four categories: A) high confidence, which indicated that further research was unlikely to change the confidence in the estimate of effect; B) moderate confidence, which indicated that further research may change the confidence in the estimate of effect; C) low confidence, which indicated that further research would likely have an important impact on the confidence in the estimate of effect; and D) insufficient, which indicated that the evidence was unavailable or did not permit a conclusion.

The customary practice of the NKF when the original diabetes guideline was published was to divide the statements into clinical practice guidelines and clinical practice recommendations. The guideline statements were based on a consensus with the Work Group that the strength of the evidence was sufficient to make definitive statements about appropriate clinical practice. When the strength of the evidence was not sufficient to make such statements, the Work Group offered recommendations based on the best available evidence and expert opinion. The original document contained five clinical practice guidelines and four clinical practice recommendations; updates for two clinical practice guidelines and one clinical practice recommendation are reported herein. The NKF now combines these statements and refers to them all as a clinical practice guideline, while specifying the strength of each recommendation and its underlying quality of evidence. Hence, Clinical Practice Recommendation 1 in the 2007 document is now referred to as Clinical Practice Guideline 6 in this update.

Rating Scheme for the Strength of the Recommendations

Grade for Strength of Recommendation in the Diabetes and CKD Guideline

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	Implications		
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Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The Work Group appreciates the careful review of the draft guideline and suggestions for improvement by external reviewers. Each comment was carefully considered and, whenever possible, suggestions for change were incorporated into the final report. As a result, this Update of the KDOQI Clinical Practice Guideline for Diabetes and CKD is the product of the Work Group, the Evidence Review Team, the National Kidney Foundation (NKF), and all those who contributed their effort to improve the updated guideline.

Individuals also provided feedback on the draft guideline during public review. Participation in the review does not necessarily constitute endorsement of the content of the report by the individuals or the organization or institution they represent.

A list of individuals who provided written review of the draft guidelines can be found in the original guideline document.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of patients with diabetes and chronic kidney disease (CKD)

Potential Harms

Risk of Hypoglycemia

- The risk of hypoglycemia is increased in patients with substantial decreases in estimated glomerular filtration (eGFR) (chronic kidney disease [CKD] stages 4 and 5) for two reasons: (1) decreased clearance of insulin and of some of the oral agents used to treat diabetes and (2) impaired renal gluconeogenesis with reduced kidney mass. The contribution of reduced renal function to the risk of hypoglycemia is difficult to quantify. About one-third of insulin degradation is carried out by the kidneys and impairment of kidney function is associated with a prolonged half-life of insulin. Patients with type 1 diabetes receiving insulin who have significant creatinine elevations (mean 2.2 mg/dL) have a 5-fold increase in the frequency of severe hypoglycemia. Therefore, it is imperative that patients being treated intensively monitor their glucose levels closely and reduce their doses of medicine as needed to avoid hypoglycemia. Progressive falls in kidney function result in decreased clearances of the sulfonylureas or their active metabolites, necessitating a decrease in drug dosing to avoid hypoglycemia. Table 4 in the original guideline document provides recommendations for drug dosing of medicines used to treat hyperglycemia in patients with CKD.
- The thiazolidinediones pioglitazone and rosiglitazone do not lead to hypoglycemia, are metabolized by the liver, and thus can be used in CKD. However, fluid retention is a major limiting side effect and they should not be used in advanced heart failure and CKD. They have been linked with increased fracture rates and bone loss; thus the appropriate use in patients with underlying bone disease (such as renal osteodystrophy) needs to be considered. The U.S. Food and Drug Administration (FDA) has restricted use of rosiglitazone based on information linking the medicine with increased cardiovascular events.

Cautions about Usage of Angiotensin-Converting Enzyme Inhibitors (ACE-Is) and Angiotensin Receptor Blockers (ARBs)

The use of ACE-Is and ARBs in early pregnancy is reportedly associated with harm to the fetus (neonatal acute kidney injury; lung toxicity; skull hypoplasia; congenital malformations of the cardiovascular system, central nervous system, and kidney), although more recent studies have not confirmed these risks. The FDA is currently reviewing its advice on the use of these agents in the first trimester.

Statins

- The FDA issued a Safety Announcement in June 2011 that recommends limited use of the highest approved dose of simvastatin (80 mg) because of increased risk of myopathy. Simvastatin 80 mg should be used only in patients who have been taking this dose for 12 months or more without evidence of muscle injury. Simvastatin 80 mg should not be started in new patients, including patients already taking lower

doses of the drug.

- The FDA has also added information to statin labels about the potential for generally nonserious and reversible cognitive side effects and reports of increased hemoglobin A_{1c} (HbA_{1c}) levels. Further information can be obtained at the [FDA Web site](#) .

Contraindications

Contraindications

- Lactic acidosis is a rare and serious side effect of metformin use, which can occur when toxic levels of metformin accumulate. Metformin is cleared by the kidneys, thus its use in chronic kidney disease (CKD) is restricted. A U.S. Food and Drug Administration (FDA) mandated black-box warning exists regarding the risk of lactic acidosis with metformin use. The label indicates that metformin should not be used in men with a serum creatinine (SCr) of ≥ 1.5 mg/dL or in women with a SCr of ≥ 1.4 mg/dL. It is also reasonable to consider a glomerular filtration rate (GFR) cutoff for metformin use as well, since SCr can translate into different estimated GFR (eGFR) levels depending on weight, race or age.
- The FDA is requiring changes to the simvastatin label to add new contraindications (concurrent cyclosporine or gemfibrozil use) and dose limitations for use with other medicines such as calcium channel blockers or amiodarone. The lovastatin label has also been updated extensively with new contraindications and dose limitations when it is taken with certain medicines that can increase the risk of myopathy; and human immunodeficiency virus and hepatitis C virus protease inhibitors are now contraindicated with simvastatin and lovastatin because of increased risk of myopathy.
- The manufacturer (Novartis) recommends that aliskiren be stopped in diabetic patients treated with angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB), and in April 2012 the FDA announced a new contraindication against the use of aliskiren with ACE-Is or ARBs in patients with diabetes because of the risk of kidney impairment, hypotension, and hyperkalemia.

Qualifying Statements

Qualifying Statements

This Clinical Practice Guideline is based upon a systematic literature search that included articles published through October 2010 and upon the best information available from relevant newer publications and scientific presentations through April 2012. It is designed to provide information and assist decision making. It is not intended to define a standard of care, and should not be construed as one, nor should it be interpreted as prescribing an exclusive course of management. Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health-care professional making use of these recommendations is responsible for evaluating the appropriateness of applying them in any particular clinical situation. The recommendations for research contained within this document are general and do not imply a specific protocol.

Implementation of the Guideline

Description of Implementation Strategy

Through collaboration with other professional organizations, including the American Diabetes Association (ADA), European Diabetic Nephropathy Study Group (EDNSG), Endocrine Society, and American Association of Clinical Endocrinologist (AACE), the National Kidney Foundation (NKF) disseminated the Guideline Update. They requested the Update either be posted on the organization's website or linked to [KDOQI.org](#) . Harmonization is essential to implementation of consistent practices that are evidence-based. Since the care of diabetic kidney disease (DKD) requires collaboration across disciplines, NKF asked that these stakeholder groups would join in promoting the importance of recognition, detection, and optimal management to reduce the risks of this devastating complication of diabetes. NKF has also secured conference presentations and press coverage, and is sending email blasts related to the key messages of the Diabetes and Chronic Kidney Disease (CKD) Update.

Implementation Tools

Foreign Language Translations

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. Am J Kidney Dis. 2012 Nov;60(5):850-86. [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2007 Feb (revised 2012 Nov)

Guideline Developer(s)

National Kidney Foundation - Disease Specific Society

Source(s) of Funding

National Kidney Foundation (NKF)

Guideline Committee

Diabetes and Chronic Kidney Disease Work Group

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Kidney Disease Outcomes Quality Initiative (KDOQI) makes every effort to avoid any actual or reasonably perceived conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the Work Group. All members of the Work Group are required to complete, sign, and submit a disclosure and attestation form showing all such relationships that might be perceived or actual conflicts of interest. This document is updated annually and information is adjusted accordingly. All reported information is on file at the National Kidney Foundation (NKF).

See *Biographic and Disclosure Information* in the original guideline document.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. Am J Kidney Dis. 2007 Feb;49(2 Suppl 2):S12-154.

Guideline Availability

Electronic copies: Available from the [National Kidney Foundation \(NKF\) Web site](#) .

Print copies: Available from the National Kidney Foundation (NKF), 30 East 33rd St., New York, NY 10016. These guidelines are also available on CD-ROM from NKF.

Availability of Companion Documents

The following are available:

- National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for diabetes and chronic kidney disease. Am J Kidney Dis. 2007 Feb;49(2 Suppl 2):S12-154. Electronic copies: Available from the [National Kidney Foundation Web site](#) .
- Management of hyperglycemia, dyslipidemia, and albuminuria in patients with diabetes and CKD: a systematic review for a KDOQI clinical practice guideline. Am J Kid Dis 2012 Nov;60(5):747-69. Electronic copies: Available to subscribers from the [American Journal of Kidney](#)

Patient Resources

The following are available:

- Diabetes and kidney disease. New York (NY): National Kidney Foundation. Available from the [National Kidney Foundation \(NKF\) Web site](#) .
- Diabetes and chronic kidney disease (stages 1-4). New York: National Kidney Foundation; 2007. 4 p. Electronic copies: Available in Portable Document Format (PDF) from the [NKF Web site](#) .
- Diabetes and chronic kidney disease (stage 5). New York: National Kidney Foundation; 2007. 20 p. Electronic copies: Available in PDF from the [NKF Web site](#) . Also available in Spanish from the [NKF Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on June 19, 2007. The information was verified by the guideline developer on August 23, 2007. This summary was updated by ECRI Institute on June 27, 2011 following the U.S. Food and Drug Administration advisory on Zocor (simvastatin). This summary was updated by ECRI Institute on April 13, 2012 following the U.S. Food and Drug Administration advisories on Statin Drugs and Statins and HIV or Hepatitis C drugs. This summary was updated by ECRI Institute on July 30, 2013. The updated information was verified by the guideline developer on August 9, 2013. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs.

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